Biotechnology

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Institute for Biological Sciences Annual Report 1990/1991

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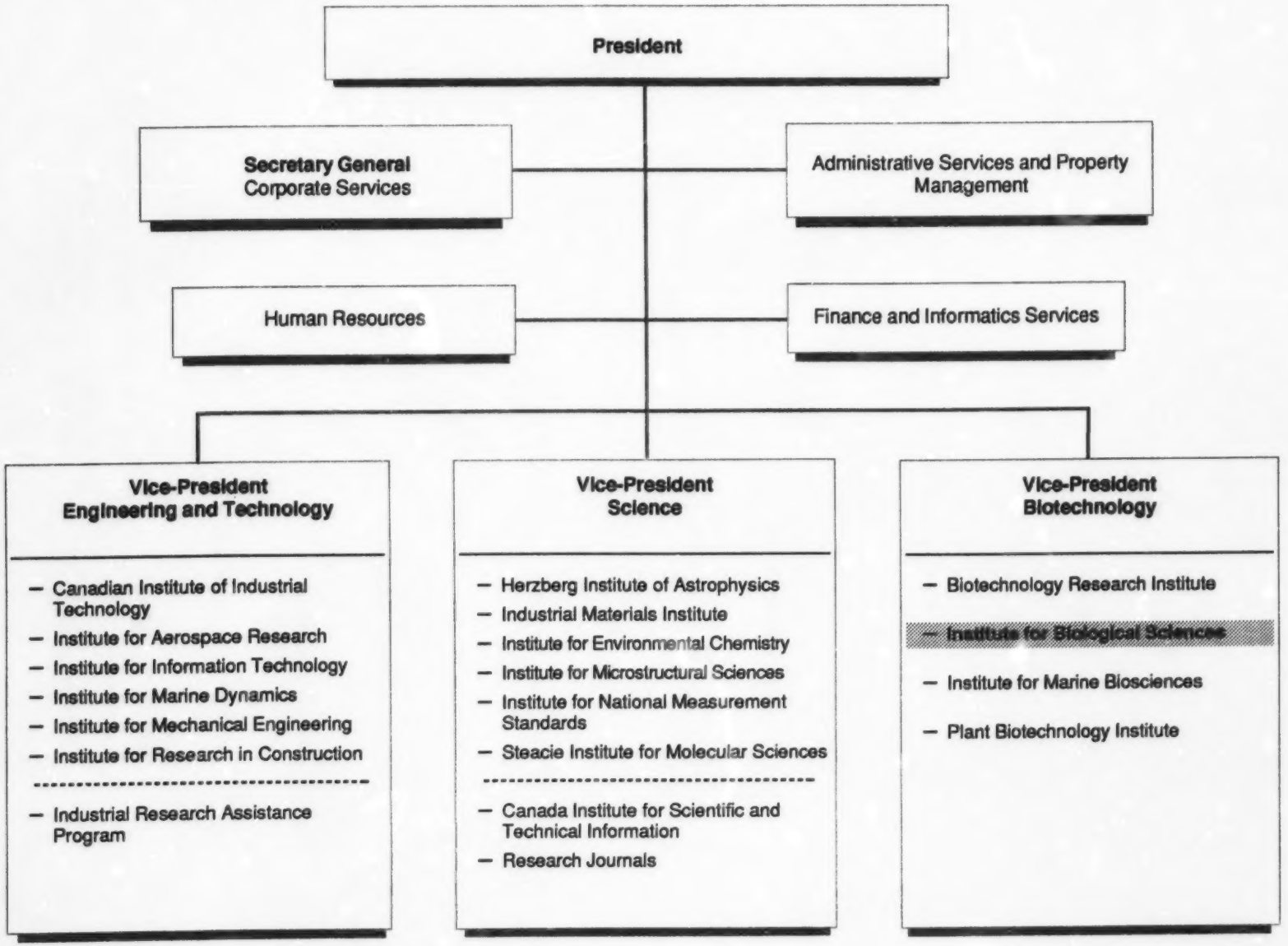
NATIONAL RESEARCH COUNCIL CANADA



Serving Canadians through Science and Engineering

The National Research Council of Canada (NRC) is the premier science and engineering organization of the Government of Canada. In 1990-91, it had an annual budget of roughly 400 million dollars and more than 3,000 employees working in research institutes and a variety of programs and facilities across the country. NRC accounts for about 10% of federal expenditures on science and technology, and provides technical advice and assistance to more than 500,000 Canadians annually.

NRC serves the needs of Canadians by helping to maintain and enhance the prosperity and competitiveness of the country through:

- the support of national science and engineering activities
- the performance of research and development
- the stimulation of investment in research and development, and
- the development and provision of vital expertise and knowledge.

To this end, NRC is both responsive and flexible, achieving its goals in partnership with others, including industry, universities and governments.

Several fundamental corporate values sustain NRC and the activities it carries out and supports:

- NRC is committed to excellence and will maintain the highest possible standards in its work
- NRC values its employees and has an historical dedication to staff excellence. It has one of the most highly qualified and experienced work forces in Canada
- NRC values innovation and strongly supports the pursuit of new developments that can improve Canada's social and economic well-being and competitiveness
- NRC values it partners and clients and knows that Canadians expect it to provide solutions to problems that have not been solved elsewhere
- NRC is committed to service to the public
- NRC supports accountability and performs its responsibilities in a manner which constantly ensures that Canada's investments in science and technology are yielding the highest national benefits.

The mission of the Institute for Biological Sciences is to perform frontier research focused on areas of mammalian biosciences that require a multidisciplinary approach, hold good potential for application, and are oriented towards Canadian social, industrial and economic development.

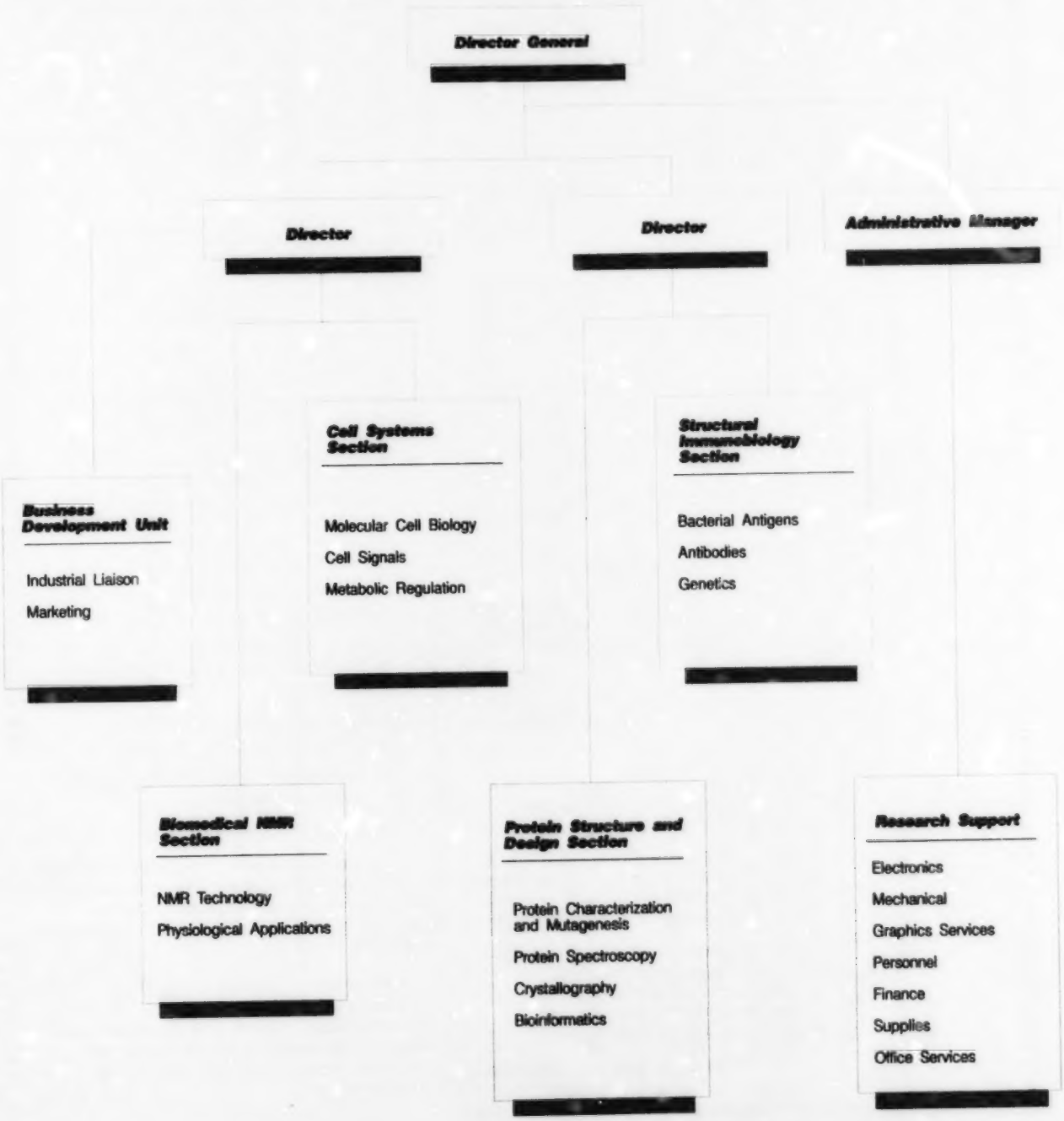
To fulfill this mission, IBS will, in partnership with scientists from industry, government, hospitals and universities:

- perform research and development related to mammalian systems including protein engineering, biomedical magnetic resonance, structural immunobiology, and molecular and cellular biology
- collaborate with and support its external partners
- seek, implement, adapt, or create the latest technology relevant to Canadian priorities
- transfer knowledge and viable techniques to appropriate partners
- provide advanced facilities and services for collaborative research
- train highly qualified personnel.

The effectiveness of IBS will be assessed on the basis of the quality and relevance of its research and development activities and outputs and its interactions with clients and partners.

Within NRC's Biotechnology Programme, IBS deals specifically with problems relating to mammalian systems and the health care industry. Its expertise lies at the frontier between the basic, clinical and applied biosciences.

Organization: Institute for Biological Sciences



Introduction

The Institute for Biological Sciences (formerly the Division of Biological Sciences) continues to maintain a balance between scientific excellence and industrial and social relevance. The past year, with a further realignment of programmes and changes in staff, has been challenging; the long list of scientific papers and of collaborations with industries and academic institutions attests to the vitality of the Institute and the capabilities of its staff to meet the challenge.

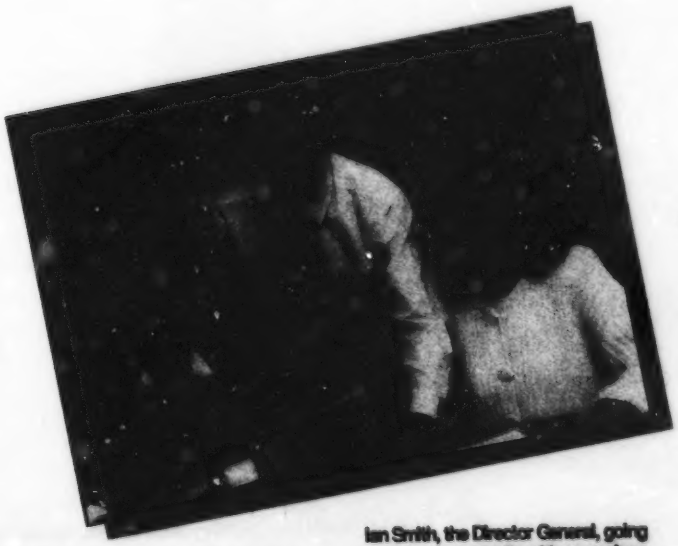
Significant scientific developments in the last year include:

- The Biomedical NMR Section's project on stroke is an excellent example of the collaborative efforts being stimulated by research expertise and facilities at IBS. Interaction between physicists and physiologists has produced techniques which have attracted medical partners from the Health Sciences Center in Winnipeg and the Loeb Institute of the Civic Hospital in Ottawa resulting in a very effective collaborative team to study the effects of stroke and therapeutic modalities using magnetic resonance imaging and spectroscopy. This multidisciplinary research team is now teaming up with pharmaceutical companies to evaluate the effectiveness of drugs in animal models and human patients.

- The Cell Systems Section has purified a novel protein, which blocks the development of normal blood cells from a patient suffering from red cell anemia and erythroblastopenia. It is believed that this protein, or related proteins, could play a significant role in the development of some aplastic anemias, erythroleukemias or other leukemias. The work involves collaboration with the Institut Gustav Roussey in Paris and the Université de Lyon. Screening of patients is being done in collaboration with the Children's Hospital of Eastern Ontario and the Ottawa Civic Hospital, and negotations are under way to involve an industrial partner in the research collaborations.

- Through the Protein Engineering Network of Centres of Excellence, the Protein Structure and Design Section is involved in research collaborations with both academic institutions and industrial partners with cysteine proteases and xylanases as areas of focus. A major collaboration with a Canadian industry has resulted in the production and characterization of parathyroid hormone. Structure/function studies at IBS are indicating the mode of action of the hormone and are indicating the way forward to a new generation of drugs to control osteoporosis.

- The Structural Immunobiology Section, in collaboration with NRC crystallographers from this Institute and the Biotechnology Research Institute, succeeded in solving the first structure of an antibody bound to its carbohydrate antigen. This 2.05Å resolution crystal structure of a *Salmonella* cell surface dodecasaccharide interacting with its monoclonal antibody provided a detailed picture of the protein-carbohydrate recognition. In conjunction with the successful expression in *E. coli* of active antibody



Ian Smith, the Director General, going over some results with co-workers Annette Kussel (left) and Thérèse Kroft.

- fragments, encoded by synthetic genes, the protein engineering loop is now complete and mutation studies of the binding site are underway.

The Institute and its Business Development Unit are increasingly pro-active and successful in attracting and expanding collaborations with industries, universities and other government departments, and in fostering technology transfer. As a result, training and collaboration contribute a large number of personnel to the Institute's research force. Some 35% of the research team are guest workers from outside collaborations. The Institute has a strong continuing interest in the training of graduate students in cooperation with local universities; a large number of our scientists hold adjunct professorships.

Financial flexibility for the Institute has been augmented by the rapidly increasing generation of revenue from sources outside NRC.

It is a tribute to our staff that so much has been accomplished in 90/91. I am proud of their scientific and industrial accomplishments and their collaborations with a wide variety of partners and clients.

Ian C.P. Smith
Director General

Anne Daley, secretary to the Director General (right) discusses arrangements with Administrative Assistant Doris Thorne (left).

The Business Development Unit

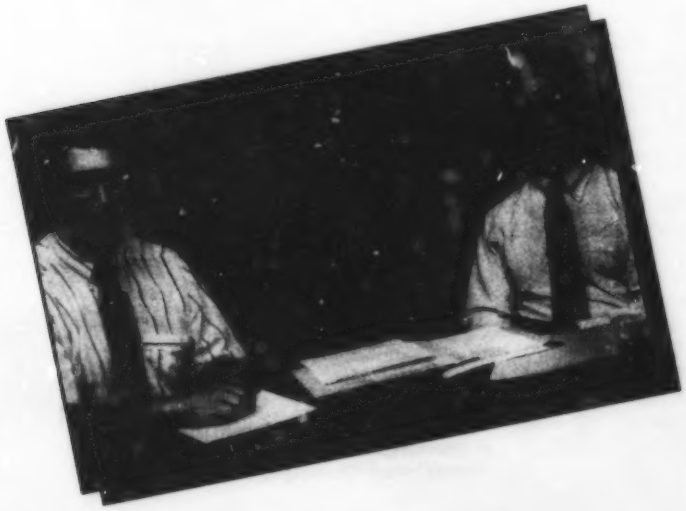
The Business Development Unit (BDU) seeks and facilitates working links between the Institute for Biological Sciences and collaborators from industries, universities, research institutions, government departments and from other NRC institutes. It responds to requests from organizations interested in collaborative research or services from the Institute and ensures that these requests are referred to the most appropriate research group.

The BDU is responsible for the transfer of new technologies generated by the Institute to industrial partners. With the assistance of NRC's Marketing Services, the BDU is active in marketing the most recent findings from the laboratories and the Institute's facilities and expertise. The BDU makes business arrangements through collaborative agreements, research contracts and service agreements.

Examples of technology licenses currently under negotiation are: a more specific assay for food contamination due to *E. coli* 0157, the causative agent for "Hamburger disease"; tests for detecting brucellosis and pleuropneumonia, infections having a commercial impact on cattle and swine production; unique analytical methods for the identification and purification of the insecticidal toxins from *Bacillus thuringiensis*, a natural and environmentally-friendly insecticide. A data storage device based on the magnetic bubble (Bernouilli) principle has been developed and licensed to a magnetic resonance equipment manufacturer. Ongoing collaborative work includes projects with Allelix Biopharmaceuticals, Bruker Spectrospin Canada Ltd., Chembiomed Ltd., F&C International Inc., IAF BioChem, International Inc., to name but a few industrial partners.

The BDU interacts with NRC's Intellectual Property Services Office to ensure that inventions by IBS scientists are effectively protected. A total of 12 patent applications have been filed by staff from the Institute for Biological Sciences to the US and Canadian Patent Offices in the last year. Once protected, the BDU ensures that these technologies are licensed and exploited commercially.

The BDU staff also promotes the various areas of expertise of the Institute. This is achieved by preparing brief outlines of newly developed technologies, as well as fact sheets describing the expertise and resources available in the Institute. With the involvement of the IBS scientists, the BDU coordinates presentations of novel findings from the laboratories to selected biotechnology companies, as well as at biotechnology trade shows and technology-transfer conferences. The main aim of the Business Development Unit is to increase the number of business and scientific opportunities where the Institute for Biological Sciences can apply its world-class technologies and skills to the benefit of Canadians.



The Business Development Unit personnel, Yves Geoffrion and Gabrielle Adams (Director, Industrial Affairs), with Marcus Brady from NRC's Marketing Services

Centre for Protein Structure and Design

NRC's Centre for Protein Structure and Design houses and coordinates the sophisticated technologies needed to determine protein structure and properties. The Centre has state-of-the-art equipment in the areas of protein crystallography, computer assisted modelling, nuclear magnetic resonance (NMR), Raman, fluorescence, circular dichroism (CD) and Fourier transform infrared (FTIR) spectroscopies.

The required personnel and capital resources are made available from the Institute for Biological Sciences in Ottawa and from the Biotechnology Research Institute in Montreal. At the same time this binodal nature of the Centre provides a unique opportunity to coordinate and focus the protein engineering programme at IBS and at BRI. Projects involving cysteine proteases, the parathyroid hormone, and the insecticidal protein from *B. thuringiensis* are examples of this approach.

The Centre actively seeks collaborations with industrial partners. Scientists from industry work at the Centre on protein engineering problems alongside NRC colleagues. Similarly, the facilities are made available to scientists from Canadian universities who spend up to one year at the Centre.

The Centre is one of the four nodes making up the Canadian Protein Engineering Network of Centres of Excellence. At the international level the Centre is linked to protein centres in the US, UK, Germany, France, Norway, Denmark, and Japan.

Biomedical NMR

Section Head R. Deslauriers
Secretary S. Firestone

Physiological Applications of NMR Group

Research Officers:
Clarke, K. (Group leader), Ally, A., Deslauriers, R., Foster, D., Geoffrion, Y., Ma, S., Preston, E., Smith, I. C.P.
Research Associates:
Nedelec, J.F.
Technical Officers:
Haas, N., Kroft, T., Lacelle, S., Mills, P., Nadeau, B.
Term Staff:
Anderson, R., Finsten, A., Morrow, R., Moore, R.
Graduate Students:
Keon, C., Tian, G., Winsborrow, B.
Guest Workers:
Lareau, S., Lukiewicz, S., Park, G. Remin, M., Racok, J., Smith, K., St. Jean, M., Stewart, L., Urbanski, A.
Summer Students:
Lawrence, D., Leddy, J., Kuprawicz, K.

NMR Technology Group

Research Officers:
Saunders, J.K. (Group leader), Butler, K.
Research Associates:
Shen, J.F.
Technical Officer:
Wessel, T.
Term Staff:
Jasinski, A.
Graduate Students:
Rapley, P., Rutter, A., Wilkins, D.
Guest Workers:
Jasinski, K., Kozlowski, P.

The Head of the Biomedical NMR Section, Roanne Deslauriers, discusses preparation of graphics with Susan Firestone.

The Biomedical Nuclear Magnetic Resonance (NMR) Section has the twin objectives of using NMR imaging and spectroscopy in non-invasive studies of physiological and pathological processes, and to develop non-invasive methods of diagnosis and evaluation of therapies for human diseases. The scientific objectives are to understand the nature and sequence of events leading to cell injury in intact organs and to develop interventions to control such processes. The application of non-invasive magnetic resonance technology for diagnosis and therapy is a response to medical needs. While the medical community perceives the need for such technology, it often does not possess or have access to the interdisciplinary scientific or technical background to develop or implement the solutions. The complexity of the problems and techniques requires a multidisciplinary team of physicists, physiologists and medical professionals which has been assembled at NRC. This team also enables NRC to maintain and expand its international standing in applications of NMR technology *in vivo*.

The Section currently works with a 89 mm bore Bruker AM-360 spectrometer (8.3 Tesla) and a 30 cm bore Bruker Biospec spectrometer/imager (4.7 Tesla). The acquisition in 1991 of a large bore (1 metre) high field magnet (3 Tesla) for the study of human subjects is a crucial step towards developing and providing new techniques and applications in biomedical NMR. As a result, the research will involve even greater interaction with medical professionals over the next five years.

Currently, investigations focus on the diagnosis and therapy of cancer, stroke and heart disease. While much research has been done with animal models, it is now expanding into studies on humans. To stay in the forefront of this medically significant field, continuing strong research is maintained in physics (NMR technology development), and in physiology, biochemistry and pharmacology.

The Section is comprised of two Groups, the NMR Technology Group which develops the technological aspects of NMR imaging and spectroscopy, and the Applications Group which uses this technology to study problems such as cancer, stroke and heart disease. The work on brain ischemia

(stroke) and heart disease focuses on defining the sequence of events which occur *in vivo* in the hours and days following interruption of blood flow and the purpose of the work is to understand cellular events in order to design more efficient therapies. Studies of ischemia (loss of flow) in heart are aimed at understanding the mechanism of cell injury. Major efforts are oriented towards obtaining quantitative information on energetics and cation movements during ischemia and reperfusion *in vitro* and *in vivo*. The program on non-invasive monitoring of preserved heart tissue aims to improve the long term viability of hearts destined for transplant. The work on cancer aims to detect, stage, and improve treatment of cancer. Studies involving tumorous tissues will allow the *in vivo* diagnosis as well as the characterization of the response of tumours to therapy.

Projects originate both within the Group and in collaboration with scientists and medical researchers in hospitals, universities and the pharmaceutical industry. The technological developments are also of continuing interest to industrial manufacturers of NMR systems, and the combination of the technology and physiological methods are of interest to pharmaceutical companies.

HIGHLIGHTS OF PROGRESS

NMR Technology

Increased resolution of NMR images is a major objective for this group. This has been achieved for small areas of the brain by the development of improved shielded gradient coils. Another significant breakthrough is the development of improved designs of shaped pulses for uniform excitation of materials using surface coils. Techniques have also been developed for acquisition of biochemical information from specific areas of the brain and heart *in vivo*. The construction and testing of a microprobe incorporating a fiber optic strain gauge for NMR studies of human heart tissue has been completed. This probe allows simultaneous measurements of the level of energy metabolites and of contractility in fresh and preserved tissues.

A special NMR probe for studies of stroke was developed by the NMR Technology Group.

To improve the reliability and accuracy of NMR spectroscopic data for clinical and medical research, progress is being made in obtaining more precise quantitative results in living systems. The development includes hardware to improve large-volume homogeneity inside NMR magnets, high-homogeneity probes, software for analysis of spectra showing large baseline distortions, and the development of non-toxic markers for determining the total amount of water and the volume of extracellular spaces.

The NMR Technology Group has recently signed a contract with a major manufacturer of NMR instruments to develop equipment for use *in vivo*.

Applications of NMR in Physiology and Medicine

Brain

Four rat models of stroke and dementia have been developed and are used for *in vivo* studies of pathology and therapy. Detrimental effects of hyperglycemia, acute caffeine, and high body temperature were demonstrated on the progression of stroke damage. Beneficial effects of mannitol, chronic caffeine, low body temperature and the drug U74006F on the outcome of stroke damage were also demonstrated. A consortium of researchers, medical practitioners, pharmaceutical companies and health care agencies is being formed to develop research programs to understand and improve therapy for stroke.

Heart

To determine the causes of cardiac injury, the isovolumically-contracting, perfused rat heart model has been developed to monitor energetics and cation movements repetitively and non-invasively during ischemia and reperfusion. Intracellular sodium concentrations were shown to increase during ischemia and this increase probably causes a large influx of calcium during reperfusion: this calcium injures the heart. The model is also being applied to studies of drug/heart

One of the surgical teams (Dominique Lawrence (left), Hong Tian and Nick Hess) participates in studies to maintain heart health during cardiac surgery.

interactions in collaboration with the pharmaceutical industry.

A number of phosphonates have been shown to be useful as internal markers for quantification of energy metabolites in heart, brain and tumors *in vivo*. Measurement of the distribution of a magnetic resonance shift reagent now allows a better assessment of cation movements during ischemia and reperfusion in intact organs.

An *in vivo* porcine model of cardiac ischemia has been developed for use with NMR methods. The model is physiologically stable and reproducible areas of infarct can be achieved without high incidence of fibrillation upon reperfusion. This model is being used to study the process of ischemic injury and to evaluate the effects of therapeutic agents. The project seeks to demonstrate differential metabolic changes in epicardial and endocardial regions of the heart following vessel restriction, and following treatment with drugs which improve heart contractility. These studies have been expanded by collaborations with medical researchers at the Civic Hospital.

Human atrial tissue and perfused pig hearts are being used to model and evaluate the best conditions for preservation of tissue to be used for transplants. The optimal temperature for maintaining energy reserves in ischemically preserved human heart tissue varies with the time of preservation. Strategies adequate for short preservation periods (less than 5 hours) are inadequate for longer times (longer than 8 hours). It was also found that high pH buffer cardioplegic solutions which improve the preservation of energy metabolites and pH in isolated human atrial appendages are of limited benefit in large, intact mammalian hearts. The fibrillation observed upon reperfusion with buffer solutions could be totally eliminated by the application of secondary cardioplegia during the warming phase prior to functional testing. This treatment also improves functional recovery of the heart.

Cancer

NMR studies of human cervical biopsies are helping to characterize the different stages of cervical anomalies. The information will be used for totally non-invasive studies of cervical and ovarian cancer at the clinical level. Improved methods for the statistical treatment of NMR data from patients have been developed based on a method known as Principal Component Analysis.

A brain tumour model , created by implanting 9L glioma cells in the rat brain, is being used to study the effects of hyperthermia, alone or in combination with chemotherapy, for the treatment of radiation-resistant brain tumours.

Clinical, non-invasive NMR studies of normal and tumorous human brain tissue are underway at the Ottawa General Hospital. In addition, surgically excised tissue is examined by high-resolution NMR to characterize its biochemistry. The project is part of a North American clinical study to investigate the use of magnetic resonance spectroscopy to characterize tumour tissue.

A rat heart is being prepared for NMR studies by Russell Anderson, visiting physician from Sweden.

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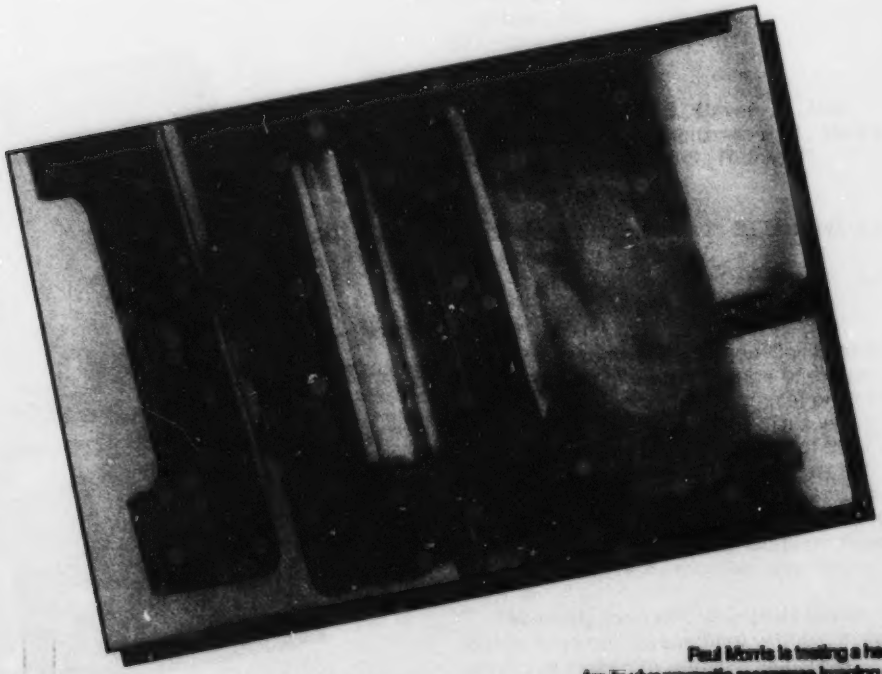

Paul Morris is testing a head coil for in vivo magnetic resonance imaging, which was built by his company, Morris Instruments Inc., in collaboration with the NMR Technology Group.

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Hepatology, 11: 65-73, 1990.

Cell Systems

Section Head J.F. Whitfield
Secretary L. Boucher

Cell Signals Group

Research Officers:
Durkin, J.P. (Group leader), Phipps, J., Rixon, R., Schwartz, J.L., Whitfield, J.F.
Technical Officers:
Dvarionas, L., Mealing, G., Isaacs, R., Tremblay, R.
NSERC Fellows:
Chakravarthy, B., Jouishomme, H.
Term Staff:
Macdonald, P., Bussey, A.
Guest Workers:
Fournier, L., MacLean, S., Morley, P.
Summer Students:
Bussey, A., Ohno, C.

Molecular Cell Biology Group

Research Officers:
MacManus, J.P. (Group leader), Czuba, M., Johnson, B., Seligy, V., Sikorska, M., Walker, P.R.
Research Associates:
Curran, I., Jahagirdar, A., Kwast-Welfeld, J., Lu, X.
Technical Officers:
Ball, R., Dove, M., Leblanc, J.M., Stephen, E. , Walker, T., Youdale, T.
Graduate Students:
deBelle, I., Hegmann, E., Schwed, P., Wood, D.
Guest Workers:
Baird, S., Calleja, G., Foster, P., Hefford, M., Shank, K.
Summer Students:
Nicholls, E.

Metabolic Regulation Group

Research Officers:
Sprott, G.D. (Group leader), Armstrong, D.W., Duff, S.J.B. , Johnson, K. , Kennedy, K.J. , Kudo, A. , Latta, R., Murray, W.D. , Overend, R.P. , Patel, G.B., Schneider, H., Velky, I. , Welsh, F.
Research Associates:
Choquet, C., Mohn, W., Ross, N.
Technical Officers:
Agnew B., Brown, L., Dicaire, C., Elliott, C.A. , Fleming, P., Labelle, J., Lamb, K. , Shaw, K.
Term Staff:
Dilawri, N.
Graduate Students:
Meakin, S.
Guest Workers:
Bruch, L., Colley, S., Davey, M., Day, J.W., Goater, A., Grenzowski, D., Merks, H., Nash, J., Porter, S., Rutten, R., Wojtczak, G.
Summer Students:
Couture, M., Francoeur, E., Howlett, J., Levesque, M., State, J.

Jim Whitfield, Section Head for Cell Systems, evaluating stages of cell differentiation with Phil Macdonald.

The recently established Cell Systems Section collects a broad range of expertise and resources to focus on critical problems in human and animal biology. This was achieved by merging parts or all of the former Molecular Genetics, Cellular Oncology, and Anaerobic Bioprocessing Groups. The Section now consists of three groups which address and focus on three major aspects of mammalian biology.

The newly formed Cell Signals Group brings together researchers with extensive expertise in mammalian cell-signalling systems. Many of the next generation of drugs and therapies will modulate cell

signalling mechanisms used by hormones, neurotransmittors, and other proteins. The Group specializes in the signals that regulate mammalian cell growth and differentiation. Research focuses on 1) identification and characterization of novel, pharmaceutically promising circulating proteins which promote or inhibit cell growth and differentiation, and 2) the mechanisms by which signals from these circulating proteins trigger crucial cellular responses.

The mandate of the Molecular Cell Biology Group is to apply advanced techniques of molecular genetics to problems of mammalian cell biology. The Group focuses on the study of the mechanisms controlling gene expression during proliferation, differentiation and programmed death in model cell systems. The Group has targeted for study some of the genes which are controlled by the cell messenger cyclic-AMP and which are likely to be involved in proliferation and differentiation. To study cell death, which is critical during embryogenesis, and in renewing populations of adult bone marrow or intestinal lining, the Group is exploiting the model of steroid- or drug-induced programmed cell death in thymic lymphocytes. This permits targeting enzymatic events for molecular studies. An entirely new initiative for the Group involves the establishment of a model of human intestinal differentiation, a process critical in the development of colorectal cancer. This cancer is the second most common in Canada.

Mammalian cell culture preparations are involved in many of the Institute's projects (B. Chakraverty, Janet MacMillan and Phil Macdonald).

The Metabolic Regulation Group develops novel products and processes based on microbial and animal cell metabolism. Emphasis is given to processes that are unique, either scientifically or technologically, as well as commercially protectable, so as to give prospective Canadian users an advantage over competitors. Projects include long term basic investigations of methane producing bacteria with a view to biomedical and industrial applications as well as a number of collaborations with industry to develop specific processes to the commercial level. The group also operates and maintains two facilities, the NRC culture collection and the cell culture laboratory, which provide highly specialized and sophisticated services to industry and to the Institute.

HIGHLIGHTS OF PROGRESS

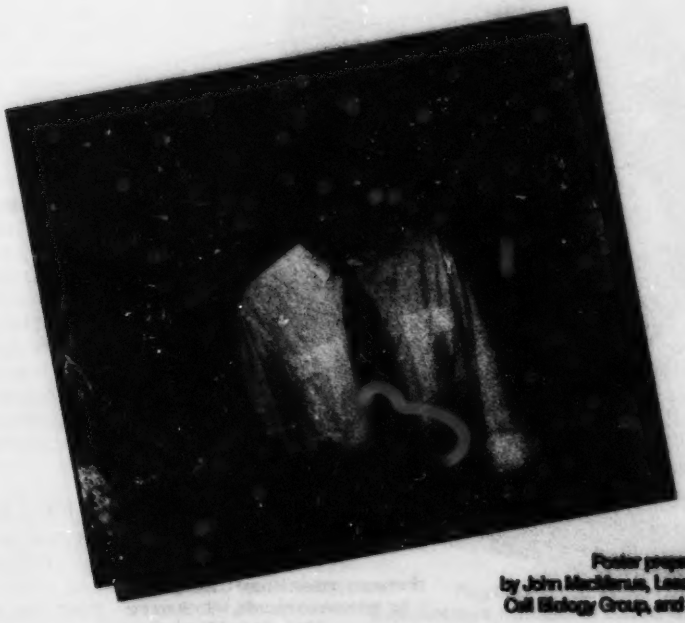
Cell Signals

Over the past year a novel protein which blocks the development of normal blood cells, has been purified to homogeneity from the blood of a patient suffering from a blood disease (pure red cell aplasia (PRCA)). The studies of this protein (Differentiation Inhibiting Protein) (DIP), are part of a major Franco-Canadian joint venture to characterize and exploit newly discovered differentiation-inhibitory factors involved in blood production. This protein, which specifically blocks the differentiation of murine and human erythroid cells, is likely responsible for the patient's anemia, and probably for other anemias as well. DIP is one of the first two proteins (an earlier discovered Autocrine Differentiation

Inhibiting Factor (ADIF) is the other) known to block blood cell differentiation without affecting cell proliferation. Cases of idiopathic PRCA frequently develop into acute leukemia. If DIP-like proteins commonly cause PRCA, their inhibition of erythropoiesis (red cell formation) may be the first in a multi-step process leading to leukemia. A collaborative program has been initiated with the Children's Hospital of Eastern Ontario to test all newly diagnosed cases of childhood leukemia for the presence of DIP-like proteins.

Studies have also indicated that DIP blocks early cellular events in the differentiation process, and that it specifically inhibits the burst of protein kinase C activity associated with the differentiation of the erythroid cells. The role DIP plays in the regulation of normal hematopoiesis, and in leukemias, is being actively pursued, in collaboration with the Franco-Canadian network.

A method to quantitate membrane-associated protein kinase C (PKC) activity directly in isolated cell membranes has now been optimized for commercialization. This PKC activity plays an extremely important role in cell growth and differentiation. The PKC assay is superior to others because it measures the activity of this important signal transducing enzyme in its native membrane environment, and can distinguish between active and inactive enzyme present on membranes. This distinction is particularly important to understanding the mechanism(s) by which membrane PKC activity is stimulated by, for example, hormones, growth factors and tumor promoters. The method has been used to show that nuclear PKC activity is rapidly stimulated in cells by phorbol esters and diacyl glycerols. The possibility that the activation of cell surface receptors can stimulate nuclear-PKC activity is currently being addressed. A collaborative effort with the Protein Engineering and Design Section has been established to make the specific PKC peptide substrate and to design inhibitors of PKC with potential industrial importance. The development of peptides that specifically recognize different isozymic forms of PKC would also have considerable commercial value.The assay's first field trial



Poster preparation is discussed by John Maclennan, Leader of the Molecular Cell Biology Group, and Marianne Sikorska.

has been the location of the PKC-stimulating domain of the parathyroid hormone (PTH) molecule. Parathyroid hormone, a small protein, plays a very important role in calcium metabolism (osteoporosis) and other vital tissue developments. The parathyroid hormone can stimulate adenylate cyclase and membrane-associated protein kinase C activity. We have now succeeded in mapping (using our new direct assay for membrane-associated protein kinase C activity) the domain of the hormone molecule needed to stimulate protein kinase C. This exciting discovery offers us, colleagues in the Protein Structure and Design Section, and an industrial partner, Allelix Biopharmaceuticals, the possibility to design and produce in quantity a new kind of parathyroid hormone for treating osteoporosis.

The Group's expertise in electrophysiology has led to the first characterization of Ca^{2+} and K^{+} channels in granulosa cells of the ovary which play a major role in the regulation of the reproductive process. It also has led to the unexpected discovery that Cl^{-} channels are involved in the mechanism by which luteinizing hormone induces progesterone secretion by these cells. It has also been found, in collaboration with BRI, that calcium and chloride channels play a role in the early events of the killing process by an insecticidal protein from *Bacillus thuringienis*. This finding perhaps represents an important clue to the mechanism of action of these natural pest-control products.

Ray Dixon (standing), discusses protein kinase C assay using rat osteosarcoma cells, with Suzanne MacLean and Rick Isaacs.

Molecular Cell Biology

We have identified and are characterising a unique 47kDa DNA-binding protein specific for genes which are controlled by cyclic-AMP. This protein, a transcription factor, is of particular interest because, unlike other related factors, it appears to be a repressor of cyclic-AMP inducible genes such as the proto-oncogene c-fos. Since defects in this control process are likely to be involved in liver cancer, we have been examining changes in these regulatory proteins in both established liver tumors and in the Farber model of experimental liver carcinogenesis. The 47kDa factor is rapidly lost during carcinogenesis and this is likely to explain, at least in part, the constitutive expression of genes such as c-fos. Since c-fos is an oncogene, it almost certainly is involved in carcinogenesis.

Suppression of the immune system is a serious side effect of many cancer chemotherapeutic drugs. We have found that this is, at least in part, due to the fact that some drugs induce normal blood forming cells to commit suicide. The mechanism by which the drugs trigger this process is being examined in order to understand the role of this cell death during normal growth and differentiation. An outcome of this work is the development of strategies to prevent the immunosuppression whilst preserving the effectiveness of these drugs against cancer cells.

It has been discovered that certain sugars, such as trehalose, act as peroxisome proliferators by regulating sequences of peroxisomal genes. Results from this work are now being applied to

explain early gene expression events in a HT29 colon cancer cell model. In addition, it has been found that trehalose breakdown can be used as a sensitive marker to measure regulatory effects of either a change of nutritional carbon source or viral infection of cells. These results encourage us to proceed to investigate both trehalose breakdown and peroxisome activity during carbohydrate induced differentiation of human intestinal cells. To this end, human DNA probes have been prepared to both trehalase and peroxisomal genes and are being used in our differentiation models.

Metabolic Regulation

Aspects of the metabolism of methane producing bacteria are distinctly different from those of other organisms, and these differences are under investigation with a view to exploiting them for the development of new products and processes. A major focus is evaluation of the central metabolic pathways as a source of unique ether lipids, and as a means of producing specifically labeled compounds.

The ether lipids of methanogens stand out by being more stable than other biologically produced lipids. Potential medical and industrial applications of this enhanced stability are under evaluation. In addition, each methanogenic species appears to have its own signature pattern of ether lipids, a relation that is of utility in their identification. The ability to use the lipids to identify the species is of practical importance. Methanogens are essential in applications such as anaerobic waste treatment, where they determine performance, and there is a need for a rapid method of identification.

Methanogens can be used to label compounds at specific points in their structure using radioactive or other marker atoms. Such compounds are expensive because they are difficult to make by the chemical procedures used presently. Hence, the possibility of making them more economically using methanogens is of potential commercial interest. Methanogens are better than other organisms at making specifically labeled compounds because of

Dennis Sprott, Leader of the Metabolic Regulation Group, measuring size distribution of liposomes made from lipids of bacteria with Chantal Dicaire.

the unusual aspect of their metabolism, where metabolic products are not recycled through major pathways. Presently, our work is focussed on an organism newly isolated in the course of the research program and which can be used to produce compounds with an unusually high degree of specificity.

A number of industrially related projects are near completion. A cell culture system was developed for optimized production of higher eukaryotic cells of interest in the production of biologicals and pharmaceuticals. Patent protection has been obtained in Canada and the U.S.A., and European and Japanese coverage is being sought. Development will continue with industrial partners. A biotechnologically-based process for the production of benzaldehyde for use as a natural flavour ("cherry-type") was developed to the commercial level in collaboration with F&C (Canada). A method developed for an industrial client is expected to increase by 25% the amount of alcohol which can be produced by fermentation of spent pulping liquor streams. The technology overcomes the effect of an inhibitor in the liquor, which otherwise prevents the fermentation of the five-carbon sugars. Canola, Canada's second largest cash crop, is grown largely for the oil present in the seeds. In the course of refining the oil, small amounts of chlorophyll have to be removed. An improved process to accomplish this has been developed for a large Canadian seed crusher and processor, CSP Foods Ltd. This process has been tested successfully at the operating plant level.

John Labelle, long time coworker with Harry Schneider, evaluates results of a fermentation process to produce alcohol from pulp waste.

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Protein Structure And Design

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Secretary: K. Hamelin

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Barber, K., Barbier, J., Hirama, T., Lanthier, P., Rollin, F., Roy, C., Watson, D., Zehab, D.
Term Staff:
McEachern, C.
Guest Workers:
Perreault, J., Stringer, K., Waseem, M.
Summer Students:
Hackam, A., Methot, N., Mui, C.

Protein Spectroscopy Group

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Paul Carey, Head of the Protein Structure and Design Section (right) and Mansuk Kim, Research Associate, adjust Laser Raman Spectroscopy equipment.

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Pippy, M. , To, R.
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Ahmed, F.R., Pippy, M., Przybylska, M.

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Research Associate:
Le, S.Y.
Computer Support:
Bramall, L., Ridgeway, J.
NSERC Fellow:
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Summer Students:
Mikulash, K.

The activities of this Section focus on "protein engineering" - an emerging technology with considerable potential for producing new materials and devices for the health-care, pharmaceutical and resource-based industries. The general approach used is based on defining the structural basis for the functional properties of a target natural protein and then using this knowledge, aided by computer calculations, to predict the effect of making changes in structure in a selected part of the protein. The changes are effected by recombinant-DNA methods and the resulting proteins are evaluated for desired properties, for example pharmacological activity. The tests may suggest further

changes in the amino-acid sequence and thus protein structure. This cycle continues until a protein is produced with superior properties in a desired application.

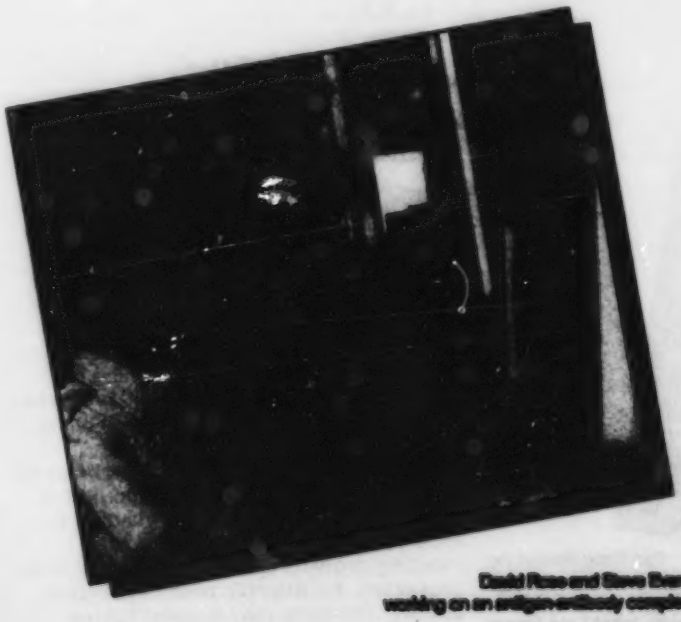
The Section is comprised of a number of groups. The Protein Spectroscopy Group provides and develops spectroscopic tools for probing protein structure and function. The spectroscopic methods include fluorescence, Raman, solid-state NMR and FTIR. Although each offers insights into one or more aspects of proteins, emphasis is given to focusing all possible techniques on the definition of the properties and mode of action of targeted proteins. To stay at the forefront of protein spectroscopy, some development of spectroscopic techniques is also undertaken. The facilities include 1) steady state and time-resolved fluorescence instrumentation, with the latter being based on a laser pumped dye-laser, 2) scanning and multichannel Raman spectrometers with a range of visible, near-UV and UV excitation sources, and 3) a Varian Unity wide bore 400 MHz solid state NMR spectrometer.

The main focus of the Bioinformatics Group is on the analysis of genetic and protein data bases and on the prediction of structure from these sequences. These activities are linked to a number of projects in the Institute and at Canadian universities. The Group also plays a central role in computing within the Institute and it is responsible for overall computer-related planning and for networking. The Group has taken the initiative in acquiring up-to-date UNIX workstations linked to a powerful multiprocessor computer that is shared by the entire Institute. In one application, the Group is now developing new computer methods to analyse difficult NMR spectra that cannot be handled by currently available commercial software.

The Protein Crystallography Group determines the three-dimensional atomic structures of macro-molecules of interest to the Institute, Canadian industries and universities, using crystallography and computer graphics techniques. The ultimate goal is to relate structure to function in order to facilitate the design of improved function-specific proteins. The Group provides liaison with the Space Agency for Canada in providing access to microgravity on space platforms for the growth of protein crystals.

The recently formed Protein Characterisation and Mutagenesis group has the broadly defined role of producing and characterising natural proteins and peptides and their mutant analogues used in the Protein Structure and Design Section. The group also provides two support functions to the Institute and outside collaborators: protein and peptide analysis and sequencing on a microgram scale, and preparation of synthetic peptides for such uses as sequence specific antibody production, hormone analogues and protease substrates. In addition, expertise is being developed, with the cooperation of BRI, on the mass spectrometric analysis of proteins and large peptides on the SCIEX ion-spray mass spectrometer. The Group also provides some assistance in circular dichroism spectroscopy with a JASCO J600 spectropolarimeter.

Although the Section has all of the elements necessary to carry out a complete protein engineering cycle, the critical mass of persons and expertise in any project is



David Rose and Steve Evans working on an antigen-antibody complex.

usually raised by strong interactions with other Sections of our Institute, with colleagues at the Biotechnology Research Institute and with the Research and Development departments of client organisations. As mentioned, the Protein Spectroscopy, the Bioinformatics and Protein Crystallography groups form part of NRC's Centre for Protein Structure and Design referred to earlier. At the national level, the Section is part of the Protein Engineering Network of Centres of Excellence (PENCE). Internationally, we are networked with protein engineering centres in Germany, USA, France, Japan, Norway, Denmark, and the United Kingdom.

HIGHLIGHTS OF PROGRESS

Spectroscopy

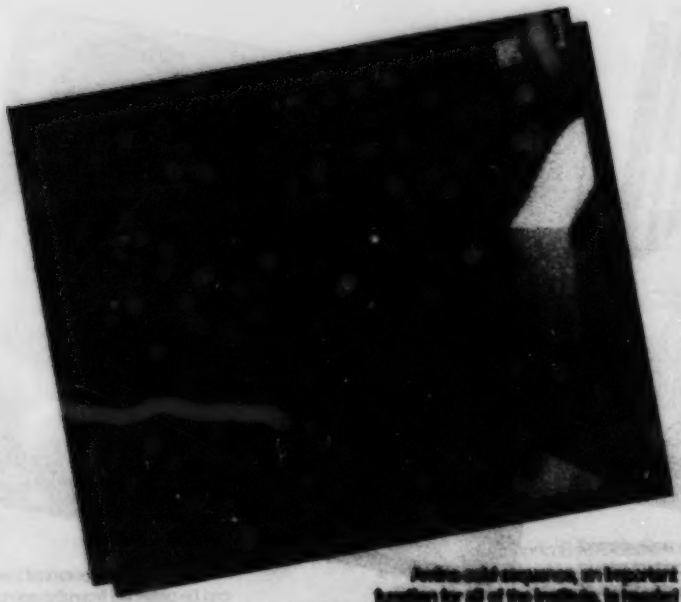
By combining resonance Raman spectroscopic and kinetic measurements of enzyme-substrate complexes under turnover conditions, it has been possible to understand the factors which provide the enzyme with its extraordinary catalytic power. Enzymes modified using protein engineering methods provided key experimental data. As a result very small changes in the lengths of bonds critical for catalytic action, of the order of 0.02Å, could be measured and related to changes in the rate of the reaction. For the first time it was possible to estimate the degree to which bond length distortion precedes the catalytic act; it was found that this distortion was about 15% of the bond length distortion needed to reach the transition state for the catalytic step.

A novel approach to mapping substrate and active-site movement has been suggested by resonance Raman studies of enzyme substrate intermediates at ambient and low temperature. An improved understanding of enzyme dynamics will facilitate the design of new purpose-based catalysts since it will show how much flexibility has to be 'built into' the active site to facilitate catalysis.

Fluorescence data from a tryptophan residue placed in different segments of the tumour protein oncomodulin indicated that binding of calcium to one of oncomodulin's two calcium binding loops stabilises the structure of the protein, while calcium binding to the second loop reorients the two loops. Knowledge of the structure of calcium binding loops was used to assist in the design of lanthanide-chelating peptides which have high potential as sensitive fluorescence probes in diagnostic applications.

The first accurate fluorescence measurements on a protein crystal were made for single tryptophan-containing myoglobin. Data for the single crystal and for myoglobin in solution were essentially identical, demonstrating the relevance of molecular dynamic calculations which use the single crystal structure as a starting point.

Pioneering solid-state two dimensional NMR studies on glycolipids showed that this approach can reveal details of lipid structure and motion in membrane systems. Another strategy involves the use of oriented lipid systems, spectral simulations and relaxation studies to provide novel insight into the molecular motions of the



Amino acid sequence, an important function for all of the Institute, is headed by Makoto Yaguchi, shown here with Camille Roy.

lipids. Similar approaches have potential for probing protein motions within a membrane matrix.

Bioinformatics

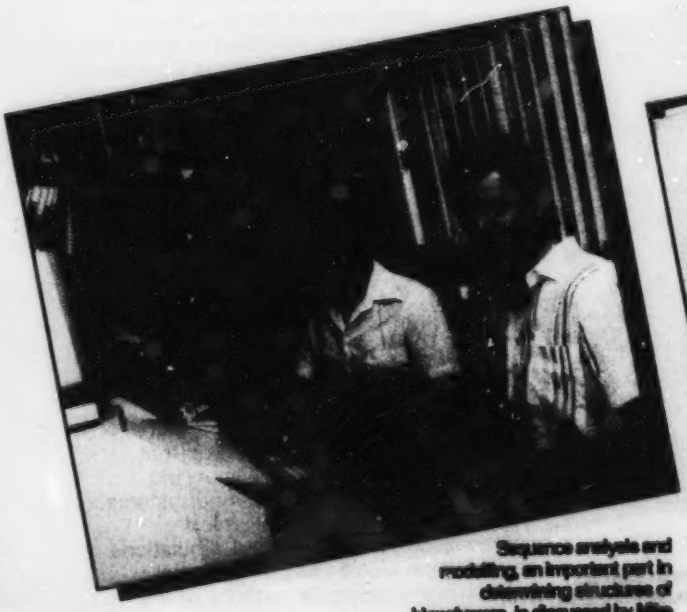
A novel mathematical technique to determine close-to-optimal solutions of dynamic programming problems has led to a powerful and effective algorithm and computer programme for predicting families of ribonucleic acid (RNA) foldings close to the computed minimum free energy. The approach has been used recently to predict common folding patterns in the 5' untranslated regions of a group of small RNA viruses, and for the RNA component in some RNA-protein complexes.

A new way to minimise differentiable functions of many variables has been developed that can overcome the multiple energy minimum problem in deducing polymer structures. It is now being applied to computing global energy minima for models of small polypeptides that approximate residues by single points. Newly acquired software allows us to perform standard molecular dynamics, energy minimisation and interactive molecular modelling. This software complements the methods being developed in-house. Currently the possible conformations of the human parathyroid hormone protein in several environments are being modelled.

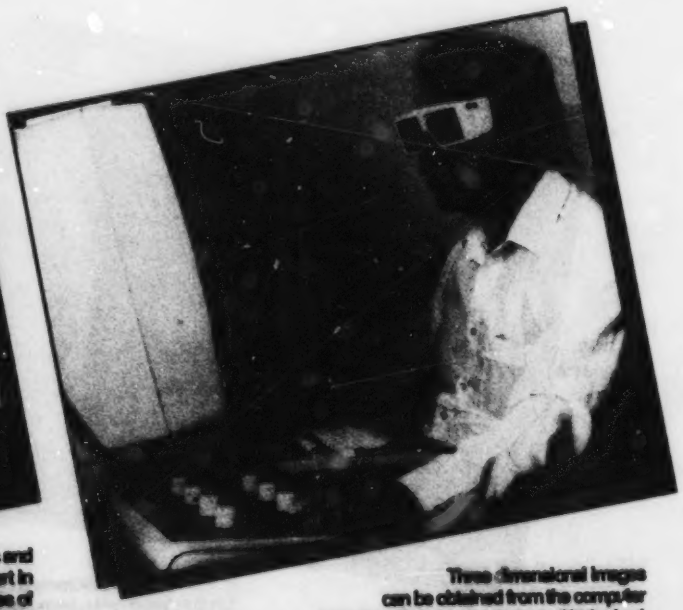
Protein Crystallography

Cathepsin B, a lysosomal cysteine protease with 30% sequence identity to papain and which is of considerable medical significance, has reached the refinement stage to 2.7Å resolution. Efforts are under way to derive atomic models for recombinant rat cathepsin B along with several inhibitor complexes.

Refinements have been completed of two antigen-binding antibody fragments (FABs) specific to polysaccharide cell-surface antigens. The unliganded FAB with affinity for the *Brucella A* antigen has been determined to 2.5Å and the structure of the antigen complex is now under analysis. In collaboration with the Biotechnology Research Institute, the antigen complex of an anti-*Salmonella* FAB has been refined to 2.1Å.



Sequence analysis and modelling, an important part in determining structures of biopolymers, is discussed by Mike Zuker (right) and Ray Somorjai.



Three dimensional images can be obtained from the computer screen by using special glasses. (Xavier Lee)

The 1.85Å structure of oncomodulin, the tumour-related calcium-binding protein, revealed an unusual inter-molecular calcium binding site that may relate to an aggregation mechanism. At present, the structure of oncomodulin is being refined further to 1.3Å resolution, using specially engineered proteins.

Protein Characterization and Mutagenesis

Native and mutant variants of parathyroid hormone (PTH), a peptide with 84 amino acid residues with potential for therapy in, for example, osteoporosis have been expressed at high levels. Improved purification procedures have been developed which allow for substantial production coupled with a high degree of purity. The procedures depend on a technique which gives high intracellular PTH expression in *Escherichia coli* in the absence of any added antibiotic, a feature with important commercial implications.

A novel analytical technique was developed to separate, identify and purify the closely related protein toxins from multigene strains of *Bacillus thuringiensis* (*Bt*), a bacterium which is the basis for environmentally benign insecticides used extensively against forest pests. The method was shown to have high potential in areas ranging from screening for new strains to monitoring production at the fermentor level.

Cathepsin B purification techniques are under development by Sadiq Hasnain and Tamako Hirama.

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Grant Bechtold, recently appointed Head of the Electronics Services function, discusses the Institute's computer network with Margaret Dunlop, Administrative Manager.

The final touches of this Annual Report are prepared by Tom Dawcett (Graphics Services) and Bert van den Berg, Director (Laboratories.)

Structural Immunobiology

Section Head D.R. Bundle
Secretary M. Leung

Bacterial Antigens Group

Research Officers:
Perry, M.B. (Group leader), Griffith, D.W., Jennings, H.J., Richards, J.C.
Research Associates:
Anderson, A.N., Beynon, L.M., Kartha, K.R.P., Kulakowska, M.
Technical Officers:
Cooper, F.P., Leitch, R.A., MacLean, L.L.
Guest Workers:
Tzianabos, A.O., Severn, W.B., Masoud, H., de Muys, J.-M., Michon, F., Pon, R.
Summer Students:
Taylor, R.

Molecular Recognition of Carbohydrate Antigens Group

Research Officers:
Bundle, D.R. (Group leader), Altman, E., Brisson, J.R., MacKenzie, C.R., Young, N.M.
Research Associates:
Auzanneau, F.-I., Baumann, H., Kihlberg, J.O., Oomen, R., Severn, W., Sigurskjold, B.W.
Technical Officers:
Eichler, E., Gidney, M.A., Johnston, R., Seguin, H., Simard, A., Sinnott, B., Webb, A.
Guest Workers:
Coffin, J., Harrison, B., Muradia, G., Peters, T., Raymond, S., Sadowska, J.M.
Summer Students:
Gagne, S., Hawara, M.

Genetics Group

Research Officers:
Narang, S.A. (Group leader)
Research Associates:
Anand, N., Brummell, D.
Technical Officers:
Bilous, D., Dubuc, G., Michniewicz, J.
NSERC Fellows:
Sharma, V.
Guest Workers:
Ma, Y.-X.
Summer Students:
MacRae, R.

David Bundle, Head of the Structural Immunobiology Section, going over a manuscript with Barry Leung.

This Section investigates the roles of complex cell surface carbohydrates and their protein receptors in disease and uses a multidisciplinary approach that combines expertise in carbohydrate chemistry, recombinant DNA technology, and gene synthesis. Research is focused on the determination of primary and three-dimensional structure of these carbohydrates and their receptors. The resulting structural knowledge provides the scientific basis for the design of new vaccines, diagnostics and, potentially, carbohydrate based therapeutics. Prominent among current problems being studied are the antibody engineering of carbohydrate binding sites and the role of 2,8-linked neuraminic acid epitopes in bacterial infections and mammalian diseases. The Section is a part of the Canadian Bacterial Diseases Network Center of Excellence, and participates through one of its members in the WHO steering committee on encapsulated bacteria, whose mandate is the search for new vaccines.

The diverse expertise available in the Section in areas of immunochemistry,

biochemistry, analytical chemistry, and synthesis, combined with expertise accessible elsewhere in Canada and abroad, continue to be used to develop novel solutions to long standing problems in clinical and veterinary microbiology, with results that are being exploited by Canadian industries. Physical resources include a level E microbial containment facility, a monoclonal antibody production unit, and an analytical laboratory providing facilities for high resolution nuclear magnetic resonance spectroscopy (Bruker AM-200, AMX-500 and AMX-600 instruments) and combined gas chromatography - mass spectroscopy. IRIS graphics workstations, microVAX 3500 and IBM mainframe computers are used for molecular modelling of carbohydrate antigens and antibodies.

The Bacterial Antigens Group focuses especially on the determination of the three dimensional structure of bacterial carbohydrate antigens of human and veterinary origin. The Group's focus on Molecular Recognition of Carbohydrate Antigens concerns itself with the interaction between these antigens and antibodies. The section is increasingly turning its attention to the role of complex carbohydrate epitopes (the small effective recognition unit that fits the binding site of the antibody) of the mammalian cell surface and their role in molecular recognition and cellular interactions, especially epitopes containing neuraminic acid. Our advances in understanding the solution conformation of 2,8-linked neuraminic acid oligomers and recent successes in crystal structure studies of antibody binding sites, including one that binds these epitopes, provide a natural avenue into this area.

Unique NRC technology for the production of polysaccharide-protein conjugate vaccines has been licensed to IAF Biochem (Montreal), and company scientists are refining this invention under the guidance of a member of the Bacterial Antigens Group. Other industrial assistance has involved antibody research as part of a Contribution Program and a Comprehensive Project with Chembiomed (Edmonton). The group also maintains close contact with industrial clients such as VIDO (Saskatoon), where confidentiality agreements have been signed for the evaluation of proprietary vaccines.

Antigen structures are being assessed by Malcolm Perry, recipient of the 1991 Canadian Society of Microbiologists Award, and Leann MacLean.

HIGHLIGHTS OF PROGRESS

Bacterial Antigens

The identification and complete structural elucidation of antigenic cell surface structures is a major part of this project, which aims to develop diagnostic tests and new vaccines against bacterial infections of human and veterinary interest. One target is the development of a new generation of subunit vaccines using chemically defined parts of the native antigen that may be derived by chemical modification or synthesis. Particular targets are diseases caused by *Neisseria meningitidis* and group B *Streptococcus* organisms.

Highlights of this work during the last year include the development of a diagnostic kit against all group B streptococcal infections, the rationale for which was based on earlier structural work by this group. Important correlations of activity with the solution properties and the

three dimensional structure of the group B meningococcal antigen were accomplished by molecular modelling studies. This antigen, an 2,8-linked homopolymer of N-acetyl neuraminic acid, can adopt a helical conformation and is closely related to epitopes that appear on mammalian adhesion molecules and certain tumours. The group B streptococcal antigen also contains neuraminic acid and resembles human tissue antigens. Recognition by the human immune system of helical epitopes in both of these capsular bacterial antigens is one way it can produce protective antibodies while simultaneously avoiding cross-reactions to self antigens.

Research on veterinary bacterial diseases identified a non-pathogenic candidate bacterial vaccine to protect against *Brucella abortus* and *Brucella melitensis*, the causal agents of brucellosis. The work of the Group has also been particularly effective in characterizing and elucidating the structures of the capsules and lipolysaccharide antigens of *Actinobacillus pleuropneumoniae*, the causal agent of swine *pleuropneumoniae* and *Pasteurella haemolytica*, the agent of cattle shipping fever.

Conjugated vaccines are being discussed by Harold [illegible] and René Karhi.

The Group is an active participant in the Canadian Bacterial Diseases Network of Centres of Excellence. As key members of the two nodes investigating Evasion of Host Mechanisms and Respiratory Diseases, the Group's staff have already obtained promising results from structural studies on the antigens and virulence factors of the human, animal and fish pathogens, *Pasteurella haemolytica, Pseudomonas aeruginosa, Klebsiella pneumoniae*, and *Yersinia ruckerii*. Two postdoctoral fellows funded by the Network are working with our NRC group; students from the University of Guelph will spend extended work periods learning techniques.

Molecular Recognition of Carbohydrate Antigens

During the last year this Group, in close collaboration with crystallographers from the IBS, succeeded in the first solution of the structure of an antibody bound to its carbohydrate antigen. This 2.05Å resolution structure of a *Salmonella* cell surface dodecasaccharide-monoclonal antibody complex revealed that aromatic amino acids dominated the binding. A branched trisaccharide epitope fills the protein site in a low energy conformation that is stabilized by intra-molecular hydrogen bonds. The protein and oligosaccharide interact through a hydrogen bond network utilizing neutral-neutral rather than neutral-charged hydrogen bonds, a result which correlates with those of functional group replacement studies.

Success in solving the first crystal structure of a bacterial antigen complexed with its antibody has provided an enormous leap forward in our understanding of polysaccharide- antibody interactions. The detailed view at the molecular level now allows us to consider altering and improving known binding sites by exploiting genetic techniques described later. Among other antigen-antibody complexes now solved or under active investigation are those from *Brucella, Shigella flexneri* and group B meningococcus.

The antigen group B meningococcus is particularly significant as it shares molecular features with several mammalian cell-surface adhesion molecules and tumour antigens. The native Fab of a monoclonal antibody to the meningococcus antigen has been solved, and crystallization trials of the antibody-oligosaccharide complex are underway. Practical applications of this work could lead to highly specific targeting reagents for therapeutic applications.

Success in this area will continue to depend on the use of advanced technologies (nuclear magnetic resonance spectroscopy, molecular graphics, X-ray crystallography and genetic engineering), and a multidisciplinary approach.

Genetics

The main goal of this Group is to understand the relationship between the amino acid sequence of antibody hypervariable loops (the part of the antibody that contacts antigen) and the resulting structure of the antigen binding site, so that we can begin to design engineered antibody sites.

The first completely synthetic Fab genes were a notable achievement of this Group late last year. The chemical synthesis involved construction of 1460 base pairs comprising the two genes encoding the *Salmonella* Fab, which have been successfully investigated by NRC protein crystallographers. Recently an active Fab of

Margaret Anne Gilday and Blair Hardman are using purification techniques for monoclonal antibodies.

Antibody gene fragments are evaluated by Steve Hwang and Ghalib Dubuc.

50kDa with correct intra- and inter-chain disulphide bonds has been efficiently expressed in *E. coli* and purified by a one-step affinity process. An active single chain variant of the antibody has also been obtained in good yield. Systematic site-directed mutagenesis of this binding site utilizing the detailed hydrogen bonding map available from the 2.05Å crystal structure, is now in progress.

The synthetic gene technology developed in this laboratory is being applied to two other carbohydrate binding antibodies. A cistronic gene of 1500 base pairs coding for the Fab of an antibody specific for *Brucella abortus* was synthesized and is being expressed in *E. coli*. Whereas the *Salmonella* antibody site was of the cavity type, the *Brucella* antibody site belongs to the other type of carbohydrate binding site, the groove type. Genes for an antibody specific to human blood group A, with as yet to be determined binding site topology, have also been synthesized for expression in *E. coli*.

Salmonella Fab gene synthesis is monitored by Carla Bilous and David Brummel.

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Animal Resources

Research Officer:
Bhasin, J.L.
Support staff:
Cleroux, M., Daoust, J., Deshney, P., Foster, M., Lapierre, J., Levert, M.

The Animal Resources main objective is to provide animals for research and veterinary services for researchers in the Institute for Biological Sciences. It also engages in collaborative research with other Sections and with outside agencies in areas of animal biotechnology.

Animal Care Services

Animal Resources is responsible for the provision of clean, disease-free animals for research carried out in the four research sections of IBS. Animal Resources achieves this goal by in-house breeding of pathogen-free animals and by procuring and maintaining animals from commercial sources.

Animal Experimentations and Veterinary Services

Special services provided are the production of immune sera against microbial, protein and synthetic antigens, production of monoclonal antibodies against PTH peptides, purification and characterisation of antibodies, and tumour transplantation in rats.

Animal Biotechnology

The development of technologies for the production of specific pathogen free laboratory animals has yielded the colony of pathogen free rabbits which is being transferred to an industrial client. This transfer of technology has resulted in significant revenue for the Institute. The company is in the process of constructing a commercial production facility in Canada.

A very significant activity is a recent collaborative project with the Cell Systems Section and the Canadian Red Cross to develop transgenic mice deficient in the gene for antithrombin III as a model for the study of thromboembolic disease and therapeutic agents against this disease.

Quality checks on SPF rabbits in the Animal Resources Facility are documented by Jagmohan Bhasin (centre), Jacques Daoust and Robert Martin.

Administration and Services

Administration

Dunlop, M., Gobey, C. *, Strang, J.
Term Staff:
Thoms, D.

Graphics Services

Devecseri, T.

Mechanical Services

Dumont, J.P., Levelle, Y., Lippke, H., Lynn, J., McFadden, P., Ruppel, A.
Term Staff:
Callaghan, B., Campbell, M., Dragic, B.

Supply Services

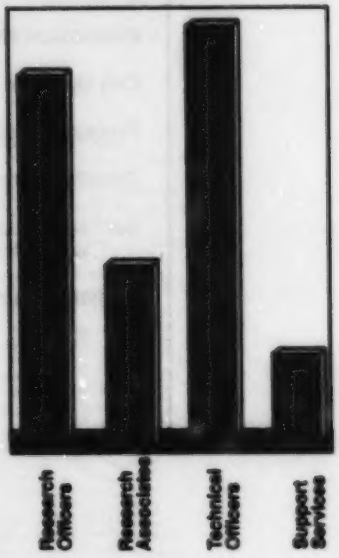
Grosser, E.E., Ashley, P., Bélec, S., Fletcher, S., Legari, J., Mould, M., Murphy, T.
Summer Student:
Clark, D.

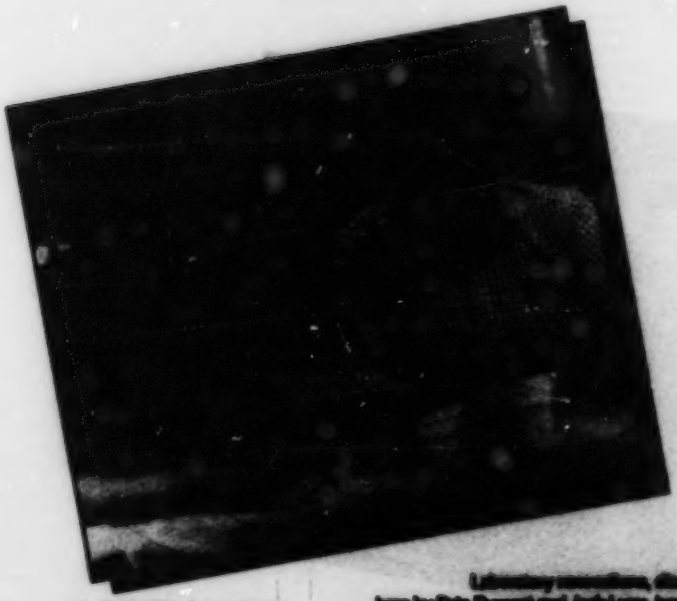
Electronics Services

Bechthold, G., Harris, D., Holmes, R., Kasperek, W., Meusser, R., Toews, R.

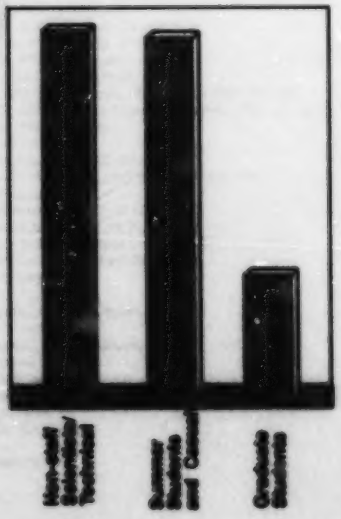
* *Deceased*

The NRC full-time staff target for the Institute in 1990/91 was 177 people. In addition, there were many guest scientists and students collaborating and working in the laboratories. This is shown by the following distributions.





Laboratory renovations, discussed here by Pete Dumont and Andi Lynn, have been a major concern of the Institute over the last few years.



Financial Statement

	Operations K$	Capital K$	Salaries M$
Biomedical NMR	300	164	1.0
Cell Systems	480	474	2.3
Protein Structure and Design	760	321	2.2
Structural Immunobiology	385	161	1.6
Sectional Support (Animal Resources, Electronics, Stores, Administration)	895	73	1.6
Facilities Maintenance	735	140	
	3555	1333	8.7

Keeping track of the Institute's operating are Ed Goosen and Margaret Mould.

Directory of Staff

TITLE	NAME	DEGREES
Director's Office		
Director-General	I.C.P. Smith	BSc, MSc (Man.), PhD (Cambridge), Fil.D. (Stockholm), D.Sc. (Winnipeg)FRSC
Executive Assistant	A. Daley	
Director (Laboratories)	L. van den Berg	BSc, MSc (Wageningen), MSc (Man.)
Director (Industrial Affairs)	G. Adams	BSc (McMaster), PhD (Carleton)
Secretary	M. Lepage	
Biomedical NMR		
Section Head	R. Deslauriers	BSc (Laval), PhD (Ottawa)
Research Officers	A. Ally	BSc (W.O.), MSc (Queen's), PhD (McGill)
	K.W. Butler	BSA (Toronto), PhD (Duke)
	K. Clarke	BSc (Flinders), PhD (Queensland)
	D.O. Foster	BSc, MSc (W.O.), PhD (Wisconsin)
	Y. Geoffrion	BSc, PhD (Laval)
	S. Ma	BSc, MSc (Hong Kong), PhD (U.B.C.)
	E. Preston	BSc, PhD (Alberta)
	J.K. Saunders	BSc (Melbourne), PhD (McMaster)
Research Associates	Shen, J.F.	MSc, PhD (Pittsburgh)
	Nedelec, J.F.	MSc (Paris XI), PhD (Paris VI)
Technical Officers	N. Haas	BSc (Ottawa)
	T. Kroft	CEGEP (Shawinigan)
	S. Lacelle	BSc (Ottawa)
	P. Mills	Dipl (Queen's)
	B. Nadeau	BSc, BA (Sir George Williams)
	T. Wessel	BSc (P.E.I.)
Secretary	S. Firestone	
Cell Systems		
Section Head	J.F. Whitfield	BSc (McGill), MSc, PhD (W.O.)
Research Officer	D.W. Armstrong	BSc, MSc (Ottawa), PhD (Carleton)
	M. Czuba	BSc, MSc (Toronto), PhD (Guelph)
	S.J.B. Duff	BSc (Guelph), MESc (W.O.), PhD (McGill)
	J.P. Durkin	BSc, PhD (Waterloo)
	B.F. Johnson	BSc (Penn. State), MA, PhD (U.C.L.A.)
	K.G. Johnson	BSc, PhD (Alberta)
	K.J. Kennedy	BSc, MSc (W.O.), PhD (Ottawa)
	A. Kudo	BSc, MSc (Kyoto), PhD (Texas)
	R. Latta	BSc (Manitoba)
	J.P. MacManus	BSc (Dublin), PhD (Lancaster)
	W.D. Murray	BSc, MSc, PhD (Waterloo)
	R.P. Overend	BSc, MSc (Salford), PhD (Dundee)
	G.B. Patel	BSc (Sardar Patel), MSc, PhD (Sask.)
	J. Phippa	DES, DEA, PhD (Toulouse)
	R.H. Rixon	BA, MA (U.B.C.), PhD (W.O.)
	H. Schneider	BSc (Sir George Williams), MSc (W.O.) PhD (McGill)
	J.L. Schwartz	Certif, EG, Adv. Studies (Grenoble) MASc, PhD (Ottawa)
	V.L. Seligy	BSc, MSc, PhD (Toronto)
	M. Sikorska	BEng, PhD (Warsaw)
	G.D. Sprott	BSc, MSc (Guelph), PhD (McGill)
	I.V. Veliky	BSc (Slovak Polytech), PhD (Slovak Acad. Sci.)
	P.R. Walker	BSc, PhD (Sheffield)
	F.W. Welsh	BSc (Manitoba), MSc, PhD (Cornell)
Research Associate	C. Choquet	BSc, MSc (Laurentian), PhD (Ottawa)
	I. Curran	BSc, MSc, PhD (Waterloo)
	A.P. Jahagirdar	MSc (Karnatak), MSc, PhD (Waterloo)
	J. Kwast-Welfeld	MSc, PhD (Warsaw)
	X. Lu	
	W. Mohn	BA (Colgate), PhD (Michigan State U.)
	N. Ross	BSc, PhD (McGill)
	M. Ujiie	BSc (Niigata), PhD (Tsukuba)
Technical Officer	B.J. Agnew	BSc (Ottawa)
	M. Ball	BSc, MSc (Carleton)
	L.A. Brown	BSc (Guelph)
	C.J. Dicaire	Dipl (Algonquin)
	M. Dove	BSc, MSc (Carleton)
	L. Dvarionas	
	C.A. Elliott	BSc (Queen's)

TITLE	NAME	DEGREES
	L.P. Fleming	BSc (Guelph)
	R.J. Isaacs	Dipl (Algonquin)
	J.L. Labelle	
	K. Lamb	BSc (Guelph)
	J.M. LeBlanc	BSc (Carleton)
	G.A.R. Mealing	BSc (Carleton)
	K. Shaw	ONC (Belfast)
	E. Stephen	BSc (Halifax)
	R.G. Tremblay	Dipl (Algonquin)
	T. Walker	Dipl (Algonquin)
	T. Youdale	BSc (Ottawa)
Secretary	L. Boucher	
Protein Structure and Design		
Section Head	P.R. Carey	BSc, PhD (Sussex)
Research Officers	G.I. Birnbaum	BS, AM, PhD (Columbia)
	S. Hasnain	BSc (Windsor), MSc, PhD (Ottawa)
	C.P. Huber	BSc, MSc (Manitoba), PhD (Oxford)
	H. Jarrell	BSc, MSc, PhD (Queen's)
	K.R. Lynn*	BSc (Adelaide), PhD (Melbourne)
	D.R. Rose	BA (Penn. State), DPhil (Oxford)
	R.L. Somorjai	BSc (McGill, PhD (Princeton)
	W.L. Sung	BSc, MSc (Oregon State), PhD (U.B.C.)
	W. Surewicz	MSc, PhD (Lodz)
	A.G. Szabo	BSc (Queen's), MA, PhD (Toronto)
	R.E. Williams	BSc, PhD (W.O.)
	G.E. Willick	BSc, MSc (U.B.C.), PhD (Illinois)
	M. Yaguchi	B.Agric. (Tokyo), MS, PhD (California)
	M. Zuker	BSc (McGill), PhD (M.I.T.)
Research Associates	R.L. Campbell	BSc (Queen's), PhD (Mass.)
	I. Clarke	BSc, PhD (U.B.C.)
	S. Evans	BSc (Heriot-Watt), MSc, PhD (U.B.C.)
	C.S. Kayden	HBSc (Lakehead), PhD (Victoria)
	M. Kim	BSc, MSc, PhD (Waseda Univ.)
	S.Y. Le	BSc (Shanghai U.), MS, PhD (Shanghai Inst.)
	X. Lee	BSc (Nanking), PhD (Grenoble)
	C. Luk	BA, MSc, PhD (U. of Rochester)
	A. Muir	BSc, PhD (U. of Calgary)
	W. Neugebauer	MSc, PhD (Gdansk)
	M. Pusztai	BSc, MSc (Debrecen), PhD (Hungarian Acad. Sci.)
	J. Randall	BSc (Memorial), PhD (U.B.C.)
	P. Tonge	BSc, PhD (Birmingham)
	K. Willis	BSc (Sheffield), PhD (Birmingham)
	W. Wakarchuk	PhD, MSc, BSc (U.B.C.)
Computer Systems	L. Bramall	
	M.E. Pippy	
	J. Ridgeway	
Technical Officers	K.M. Barber	BSc (Carleton)
	J.R. Barbier	Dipl (Algonquin)
	R.G. Carriere	Dipl (Chem. Inst.)
	T. Hirama	BSc (Tokyo)
	D.T. Krajcarski	Dipl (Manitoba Inst. Technol.)
	P.H. Lanthier	Dipl (St. Lawrence)
	T. Lessard	Dipl (Algonquin)
	C.F. Rollin	Dipl (Hull Tech.)
	C. Roy	Dipl (Hull Tech.)
	L. San Cartier	
	R. To	BSc (National Taiwain U.)
	L. Turner	
	D.C. Watson	BSc (Brighton)
	D.M. Zahab	C.E.T. (Algonquin)
Secretary	K. Hamelin	
Structural Immunobiology		
Section Head	D.R. Bundle	BSc (Nottingham), PhD (Newcastle)
Research Officers	E. Altman	BSc, MSc (Jerusalem), PhD (U.B.C.)
	J.R. Brisson	BSc, MSc (Ottawa), PhD (Toronto)
	D.W. Griffith	BSc (Guelph)
	H.J. Jennings	MSc, PhD (Queen's)
	C.R. MacKenzie	BSc (Acadia), MSc, PhD (Guelph)
	S.A. Narang	BSc, MSc (Panjab), PhD (Calcutta), FRSC
	M.B. Perry	BSc, PhD, DSc (Bristol), FRSC
	J.C. Richards	BSc, PhD (McMaster)

TITLE	NAME	DEGREES
	N.M. Young	BSc, PhD (Birmingham)
Research Associates	N.N. Anand	BSc (Panjab), MSc (Chandigarh), PhD (Cambridge)
	A.N. Anderson	BSc, PhD (Rhodes)
	F.-I. Auzanneau	DEA, PhD (Paris)
	H. Baumann	BSc, PhD (Stockholm)
	L. Baynon	BA (Open), MSc, PhD (U.B.C.)
	D. Brummall	BSc (Nottingham), PhD (Sussex)
	K.R.P. Kartha	BSc, MSc (Kerala), PhD (Gujarat)
	J. Kihlberg	MSc, PhD (Lund)
	E. Kulakowska	MSc (Wroclaw), PhD (Polish Acad. Sci.)
	R. Oomen	BSc, PhD (Ottawa)
	W. Severn	BSc, PhD (Victoria)
	B.W. Sigurskjold	BSc (Copenhagen), MSc (Carlsberg), PhD (Denmark)
Technical Officer	D. Bilous	BSc (Marianapolis)
	F.P. Cooper	
	G. Dubuc	Dipl (Cdn. Soc. Lab. Tech.)
	E. Eichler	MSc (Chem. Technol.)
	M.A.J. Gidney	BSc, MSc (Acadia)
	R.A.Z. Johnston	BSc, MSc (Manitoba)
	R.A. Leitch	BSc (Guelph), MSc (Ottawa)
	L. MacLean	Dipl (Ryerson)
	J.J. Michniewicz	Dipl (Ryerson)
	H. Seguin	
	A. Simard	Dipl. (Algonquin)
	B. Sinnott	
	A. Webb	BSc (Liverpool)
Secretary	M. Leung	
Animal Resources		
Group Leader	J.L. Bhasin	BVSc, MVSc (Jabalpur), PhD (Davis)
Research Animal Care	M. Cleroux	
	J. Daoust	
	P. Dashney	
	M. Foster	
	J. Lapierre	
	M. Levert	
Administration and Services		
	M.V. Dunlop	Administrative Manager
	C. Gobey*	Personnel Clerk
	J. Strang	Administrative Assistant
	D. Thoms	Personnel Clerk
High Technology Services		
	G. Bechthold	Associate Research Officer
	D. Harris	Technical Officer
	R. Holmes	Technical Officer
	W. Kasperek	Technical Officer
	R. Mausser	Technical Officer
	R. Toews	Technical Officer
Mechanical Services	J.P. Dumont	Technical Officer
	P.W. McFadden	Technical Officer
	Y. Leveille	Technical Officer
	H. Lippke	Technical Officer
	J. Lynn	Technical Officer
	A. Ruppel	Technical Officer
Graphics Services	T. Devecseri	Photographer
Supply Services	E.E. Grosser	Supply Officer
	S. Fletcher	Supply Clerk
	P. Ashley	Supply Clerk
	J. Legari	Supply Clerk
	S. Belec	Supply Clerk
	M. Mould	
	T. Murphy	Supply Clerk

* Deceased.

Research Facilities

- Fermentation facility ('C' level containment) - 0.5 L to 250 L fermentors. Tangential flow membrane harvest equipment as well as high capacity continuous flow centrifuges. Large volume 18 megohm water generation module.
- Pathogen containment and fermentation facility - 28 L and 75 L fermentors with cell harvesting equipment for culturing pathogenic organisms.
- Culture collection - in-house collection of more than 2500 species of bacteria, yeast and fungi, most of them available on request.
- Animal facility - specific pathogen free and gnotobiotic mice, rats and rabbits; nude mice, and conventional animals for research purposes.
- Nuclear magnetic resonance (NMR) - 600, 500, 360 (2), 200 MHz high resolution instruments; 400, 300, 200 MHz broad line instruments; 200 MHz, 30 cm horizontal bore, whole body instrument for spectroscopy and imaging; 130 MHz, 1 meter horizontal bore, whole body instrument for spectroscopy and imaging.
- X-ray diffractometer with area detector.
- Raman spectroscopy - lasers and spectrographs for Raman spectroscopy in the visible and near-uv regions.
- Steady state and laser-based time resolved fluorescence instrumentation.
- Circular dichroism spectroscopy (uv and visible) - Jasco J600, thermostatted.
- Computers - Silicon Graphics 4D/280 (8 processors) Unix Server linked to the campus-wide ethernet network (TCP/IP and Decnet) for 10 MB communication and data transfer (locally) and 56 KB (externally). This server will soon contain protein and DNA databases and Molecular Biology Unix-based computing applications. Currently supports Institute's computing for memory- and cpu- intensive applications. VAX 11/750 supports Evans and Sutherland PS300 graphics system and other VAX/VMS software applications.
- Molecular Graphics Systems (Unix-based) - Evans and Sutherland (ESV 10), and Silicon Graphics (IRIS 4D/70GT, 4D/25G, 4D/35G).
- Amino acid sequenator - Applied Biosystem, gas phase (2); Beckman 890, liquid phase (2).
- Amino acid analyzer - Durrum D500.
- Peptide synthesizer - BioSearch Sam II, Milligen/BioSearch 9050.
- DNA synthesizers - BioSystems (2).
- Cation biofluorometer - Spex CM system specificity for intracellular $Ca2^{+}$.
- Stereotaxic apparatus and microinjection capability.
- Cytofluorographic facility (flow cytometry and cell sorting).
- Mammalian cell culturing laboratory.
- Hybridoma production laboratory.
- Titration microcalorimeter.
- Double focusing high resolution mass spectrometer.
- GC-MS general purpose spectrometer.
- Submicron particle sizer.
- Semi-automated DNA sequencing - Applied Biosystems Model 3T3A.
- Multiple peptide synthesis with peptide derived polyclonal antibody production.
- Pulsed-field separation of mega DNA fragments.
- Multi-species DNA electroporation.

Research Partnerships

The Institute is involved in many collaborative research projects with industry, academic institutions and other government departments, and staff also participate extensively in outside activities, as indicated by the following lists:

Research collaborations with industry:

Company	*Section*	*Institute Staff*
Aastra Aerospace	Protein Structure and Design	G. Birnbaum D. Rose
Advanced Membranes	Protein Structure and Design	W. Sung
Allelix Biopharmaceuticals	Cell Systems	J.F. Whitfield R.H. Rixon
	Protein Structure and Design	W.L. Sung G.E. Willick A.G. Szabo D.R. Rose
Alliance Pharmaceuticals	Biomedical NMR	R. Deslauriers
Better Yield Insects	Cell Systems	I. Veliky
Bio-Research Laboratories	Biomedical NMR	A. Ally
Bruker Spectrospin Canada Ltd.	Biomedical NMR	J.K. Saunders I.C.P. Smith
Canadian Bank Note Company	Protein Structure and Design	A.G. Szabo
Chembiomed Ltd.	Structural Immunobiology	D.R. Bundle
Connaught Laboratories	Protein Structure and Design	G. Birnbaum D. Rose
ICI Canada	Protein Structure and Design	P.R. Carey M. Pusztai
Convex Computer Corp.	Protein Structure and Design	M. Zuker
CSP Foods Limited	Cell Systems	H. Schneider
Digital Equipment Corporation	Protein Structure and Design	M. Zuker
Diversified Research Laboratories, George Weston Group of Companies	Cell Systems	B. Patel G.D. Sprott
F&C International	Cell Systems	D.W. Armstrong
Forintek Canada Corp.	Protein Structure and Design	G.I. Birnbaum D.R. Rose
IAF BioChem International Inc.	Structural Immunobiology	H.J. Jennings
Kronem Systems Inc.	Cell Systems Protein Structure and Design	J.P. MacManus A.G. Szabo
Iogen Corp.	Cell Systems Protein Structure and Design	V.L. Seligy W. Sung G. Willick M. Yaguchi
Labatts Brewing Company Limited	Cell Systems	V.L. Seligy
New England Biologicals	Cell Systems	G.D. Sprott G.B. Patel
Nordion	Cell Systems	J. Durkin
Ottawa Virology	Cell Systems	D. Armstrong

Research collaborations with industry (Cont'd):

Company	*Section*	*Institute Staff*
Paprican (Centres of Excellence)	Cell Systems Protein Structure and Design	V.L. Seligy P.R. Carey D.R. Rose G.E. Willick M. Yaguchi W.L. Sung
Paques Lavalin	Cell Systems	K.J. Kennedy A. Kudo
ParaDigm Biotechnologies	Cell Systems	D.W. Armstrong J.F. Whitfield
Pegasus Biotechnology	Cell Systems	D.W. Armstrong
Philom Bios	Cell Systems	I. Veliky
Quesnel River Pulp Company	Cell Systems	K.J. Kennedy A. Kudo
Rhône-Poulenc	Biomedical NMR	J.K. Saunders K. Clarke
Sepracor Inc.	Structural Immunobiology	D.R. Bundle
Siemens Electric Ltd.	Biomedical NMR	I.C.P. Smith J.K. Saunders
Syntex Canada (Centres of Excellence)	Protein Structure and Design	P. Carey S. Hasnain C.P. Huber
Temfibre	Cell Systems	H. Schneider
Varian Canada, Inc.	Protein Structure and Design	H.C. Jarrell
Vetech	Cell systems	B. Johnson V. Seligy
Veterinary Infectious Diseases Organization	Structural Immunobiology	E. Altman D.R. Bundle
	Protein Structure and Design	M.B. Perry M. Yaguchi D. Rose

Research collaborations with academic institutions:

Institution	*Section/Topic*	*Institute Staff*	*Number of Students in Inst.*
Brown University, Rhode Island	Protein Structure and Design	P.R. Carey	
Carleton University	Cell Systems	D.W. Armstrong	2
		G.D. Sprott	1
	Structural Immunobiology	S.A. Narang	1
	Cell Systems	V.L. Seligy	3
	Biomedical NMR	J.K. Saunders	2
		I.C.P. Smith	
		A. Ally	
Carlsberg Institute, Denmark	Structural Immunobiology	D.R. Bundle	
Guelph University	Cell Systems	V.L. Seligy	
Health Sciences Centre, Winnipeg	Biomedical NMR	J.K. Saunders	
		I.C.P. Smith	

Research collaborations with academic institutions (Cont'd):

Institution	*Section/Topic*	*Institute Staff*	*Number of Students in Inst.*
Heart and Stroke Foundation of Ontario	Biomedical NMR	R. Deslauriers	2
Institute of Nuclear Physics, Poland	Biomedical NMR	J.K. Saunders I.C.P. Smith	
Karolinska Institute	Structural Immunobiology	D.R. Bundle	
Loeb Research Institute, Ottawa	Cell Systems	J.L. Schwartz	
McGill University	Protein Structure and Design	W.L. Sung	
Networks of Centres of Excellence	Structural Immunochemistry Protein Structure and Design	M.B. Perry and others P.R. Carey and others	
NIH-Brigham Women's Hospital	Structural Immunobiology	H.J. Jennings	
Ontario Cancer Clinic	Biomedical NMR	J.K. Saunders I.C.P. Smith R. Deslauriers	
Ottawa Heart Institute	Biomedical NMR	R. Deslauriers	1
Queen's University	Cell Systems	J.F. Whitfield	
Scripps Institute	Cell Systems	M. Sikorska	
St. Michael's Hospital, Toronto	Biomedical NMR	R. Deslauriers	
State University of New York	Protein Structure and Design	M. Zuker	
Stockholm University	Biomedical NMR	I.C.P. Smith	
Université du Quebec à Montréal	Biomedical NMR	E. Preston R. Deslauriers	
University of Alberta	Cell Systems	J.P. MacManus	
University of British Columbia	Protein Structure and Design Cell Systems	M. Yaguchi V.L. Seligy	
University of California at San Diego	Protein Structure and Design	S. Hasnain	
University of Coimbra, Portugal	Protein Structure and Design	P.R. Carey	
University of Florida at Gainsville	Cell Systems	G.B. Patel	
University of Frankfurt, Germany	Structural Immunobiology	J.-R. Brisson	
University of Guelph	Cell Systems	G.D. Sprott G.B. Patel	
	Protein Structure and Design	M. Zuker	
University of Manitoba	Biomedical NMR	I.C.P. Smith J.K. Saunders E. Preston	
	Structural Immunobiology	J.C. Richards	
University of Missouri, St. Louis	Protein Structure and Design	C.P. Huber	
University of Montreal	Structural Immunobiology Cell Systems	E. Altman J.L. Schwartz	
University of Ottawa	Cell Systems	K.J. Kennedy	2
		G.D. Sprott J.P. Durkin	2
		J-L. Schwartz	3
		J.F. Whitfield J.P. MacManus	
		M. Sikorska	1

Research collaborations with academic institutions: (Cont'd)

Institution	*Section/Topic*	*Institute Staff*	*Number of Students in Inst.*
University of Ottawa (Cont'd)		P.R. Walker	
		V.L. Seligy	
	Biomedical NMR	R. Deslauriers	6
		A. Ally	
		K. Butler	
		K. Clarke	1
		I.C.P. Smith	2
		J.K. Saunders	
		Y. Geoffrion	
	Protein Structure and Design	P.R. Carey	4
University of Sherbrooke	Cell Systems	J.L. Schwartz	
University of Toronto	Biomedical NMR	R. Deslauriers	
University of Rochester	Protein Structure and Design	M. Zuker	
University of Sydney	Biomedical NMR	I.C.P. Smith	
Wayne State University	Protein Structure and Design	S. Hasnain	
Yale University	Protein Structure and Design	G.I. Birnbaum	

Research collaborations with other national and international government institutions:

Institution	*Section*	*Institute Staff*
Agriculture Canada	Structural Immunochemistry	J.C. Richards
	Protein Structure and Design	R.E. Williams
	Cell Systems	V.L. Seligy
	Protein Structure and Design	M. Yaguchi
	Biomedical NMR	K. Clarke R. Deslauriers
	Cell Systems	I. Valiky
Canadian Institute for Advance Research	Protein Structure and Design	M. Zuker
Civic Hospital (Loeb Inst.)	Biomedical NMR	E. Preston
CNRS, France	Cell Systems	J.P. Durkin J.F. Whitfield M. Sikorska
	Structural Immunobiology	M.B. Perry
	Protein Structure and Design	I.C.P. Smith H.C. Jarrell
Department of National Defence	Cell Systems	D.W. Armstrong
	Structural Immunobiology	D.R. Bundle
Environ. Protection Agency , USA	Cell Systems	J.L. Schwartz
Forestry Canada	Protein Structure and Design	M. Puaztai P.R. Carey
Gov't. of Ontario, Premier's Council Technology Fund	Biomedical NMR	I.C.P. Smith
	Cell Systems	V.L. Seligy

Research collaborations with other national and international government institutions: (Cont'd)

Institution	*Section*	*Institute Staff*
	Structural Immunobiology	M. Young
Health & Welfare Canada	Cell Systems	D.W. Armstrong
	Structural Immunobiology	M.B. Perry H.J. Jennings N.M. Young
	Cell Systems	V.L. Seligy
IDRC/Indian Institute of Technology, Bombay, India	Cell Systems	K.J. Kennedy
	Cell Systems	G.B. Patel
INRA, France	Structural Immunobiology	D.R. Bundle J.C. Richards
Institute for National Standards	Cell Systems	P.R. Walker
Institut Laue-Langevin	Protein Structure and Design	X. Lee
International Network Protein Engineering Centres	Protein Structure and Design	P.R. Carey
Karolinska Institute, Sweden	Biomedical NMR	I.C.P. Smith R. Deslauriers
	Structural Immunobiology	D.R. Bundle
Louis Riel High School	Biomedical NMR	R. Deslauriers
Lester B. Pearson High School	Biomedical NMR	R. Deslauriers
National Institute of Health, USA	Structural Immunobiology	H.J. Jennings
	Protein Structure and Design	R.L. Somorjai
	Biomedical NMR	R. Deslauriers
Ottawa Civic Hospital	Biomedical NMR	E. Preston I.C.P. Smith
	Cell Systems	J.P. Durkin J.F. Whitfield J.L. Schwartz M. Sikorska P.R. Walker
	Protein Structure and Design	A.G. Szabo
Ottawa General Hospital	Biomedical NMR	J.K. Saunders I.C.P. Smith
Shriners Hospital/ McGill University	Protein Structure and Design	S. Hasnain C. Huber
Steacie Inst. for Molecular Sciences	Cell Systems	M. Sikorska

Organizational activities outside NRC:

Institute Staff	*Organization/Journal*	*Role*
Ally, A.	BioResearch Laboratories Ltd.	Advisor
Bundle, D.R.	Chembiomed	Advisor
	American Chemical Society	Symposium Organizer
	Carbohydrate Research	Member, Editorial Board
	Int'l Journal for Biological Macromolecules	Member, Editorial Board
	Centre for Complex Carbohydrates, Athens, GA	Member, Scientific Advisory Board
Carey, P.R.	Int'l Conferences on Raman Spectroscopy	Advisory Committee
	Int'l Conferences on Interaction of Laser Light on Biological Objects	Advisory Committee
	Conference on Enzymes in Biotechnology	Advisory Committee
	European Conference on Spectroscopy in Biology	Advisory Committee

Organizational activities outside NRC: (Cont'd)

Institute Staff	*Organization/Journal*	*Role*
	Conference on Spectroscopy in Biology	Symposium Organizer
	Int'l Biophysics Satellite Meeting	Symposium Organizer
	NSERC Committee on International Relations	Member
	International Network Protein Engineering Centres	NRC/Canadian representative
Clarke, K.	NMR in biomedicine	Editorial Board
Deslauriers, R.	Int'l Society for Magnetic Resonance (ISMAR)	Member of Council
	ISMAR, Division of Biology and Medicine	Member, Steering Committee
	External Ventricular Assist Device	Member, Scientific Review Committee
	Canadian Journal of Spectroscopy	Associate Editor
	NMR in Biomedicine	Member, Editorial Board
	Resonance	Editor
	Society for Magnetic Resonance in Medicine	Member of Board of Trustees
Foster, C.D.O.	Canadian Journal of Physiology and Pharmacology	Associate Editor
Jennings, H.J.	IAF Biochemicals	Advisor
	World Health Organization	Expert
	16th Int'l Congress of Chemotherapy	Symposium Organizer
Kennedy, K.J.	BIOQUAL Network	Secretary
	World Energy Congress	Committee Member
Narang, S.A.	International Centres of Genetic Engineering and Biotechnology	Member, Panel of Scientific Advisors
	Methods in Molecular and Cellular Biology	Member, Editorial Board
Patel, G.B.	Canadian Journal of Microbiology	Associate Editor
	Canadian Society of Microbiologists	Microbial Physiology Section Chairperson
	Canadian Society of Microbiologists	Symposium Organizer
	Environment Canada	Expert Input CEPA Regulations affecting Biotechnology
	Univ. of Saskatchewan	External Examiner Ph.D. Thesis
	Ottawa Bacteriology Club	President
Schwartz, J.L.	Spex Industries	Advisor
	Imaging Research	Advisor
Seligy, V.L.	Premier Council, SCITEC	Scientific Advisor
	University of Toronto, Institute of Biotechnology	Member, Advisory Board
	Int'l Committee Iridoviruses	Associate Chairman, Advisory Board
	MRC Fellowship Committee	Associate Chairman
	NSERC (CRD) Grants	Scientific Advisor
	ISTC	Scientific Advisor
	IRAP	Scientific Advisor
Sikorska, M.	International Union for Biological Sciences	Member, Canadian National Committee
Smith, I.C.P.	Biophysical Society of Canada	President
	Society for Magnetic Resonance in Medicine	Executive Committee
	Int'l Union of Pure and Applied Biophysics	Program Chairman, 10th Biophysics Congress
	Canadian National Committee on Biophysics	Chairman
	Western Psychiatric Hospital, Pittsburgh	Advisor
	Journal of Magnetic Resonance	Editorial Board
	Magnetic Resonance in Chemistry	Editorial Board
	Molecular Pharmacology	Editorial Board
	Molecular and Cellular Biochemistry	Editorial Board
Sprott, G.D.	Canadian Journal of Microbiology	Section Editor
	Journal of Bacteriology	Editorial Board
Walker, P.R.	International Conference on Alzheimer's Disease	Advisory Committee
Zuker, M.	Canadian Institute for Advanced Research	Fellow
	Computer Applications in the Biological Sciences	Member, Editorial Board